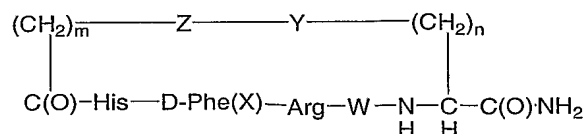


## WHAT IS CLAIMED IS:

1. A method of inhibiting alcohol consumption comprising administering a therapeutically effective amount of a selective melanocortin 4 receptor agonist to a subject in need thereof wherein the selective melanocortin 4 receptor agonist is a compound of Formula I:



I

wherein:

His is L-histidyl;

D-Phe(X) is D-phenylalanyl unsubstituted or optionally para-substituted with a group selected from F, Cl, Br, Me, and OMe;

Arg is L-arginyl;

W is L-tryptophanyl or 2-naphthyl-L-alanyl;

one of Y and Z is  $\text{--C(O)--}$  and the other is  $\text{--NH--}$ ;

m is 1 to 4;

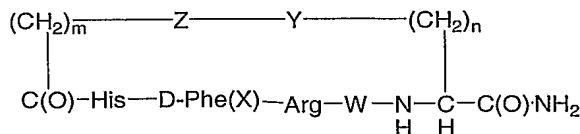
n is 1 to 4, provided that  $n+m$  is 4 to 6; or

a pharmaceutically acceptable salt thereof.

2. The method of Claim 1 wherein Y is  $\text{--C(O)--}$  and Z is  $\text{--NH--}$ .

3. The method of Claim 2 wherein m is 2 and n is 2.

4. The method of Claim 3 selected from:



Z	Y	X	W	m	n
NH	C(O)	H	Trp	4	2
NH	C(O)	H	Trp	3	2

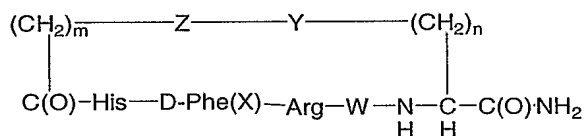
Z	Y	X	W	m	n
NH	C(O)	H	Trp	2	2
NH	C(O)	H	Trp	1	2

or a pharmaceutically acceptable salt thereof.

5. The method of Claim 4 selected from cyclo(NH-CH<sub>2</sub>-CH<sub>2</sub>-CO-His-D-Phe-Arg-Trp-Glu)-NH<sub>2</sub>, or a pharmaceutically acceptable salt thereof.

5

6. A method of reducing alcohol consumption comprising administering a selective melanocortin 4 receptor agonist, or a pharmaceutically acceptable salt thereof, to a subject in need thereof wherein the selective melanocortin 4 receptor agonist is a compound of Formula I:



10

I

wherein:

His is L-histidyl;

D-Phe(X) is D-phenylalanyl unsubstituted or optionally para-substituted with a group selected from F,

15 Cl, Br, Me, and Ome;

Arg is L-arginyl;

W is L-tryptophanyl or 2-naphthyl-L-alanyl;

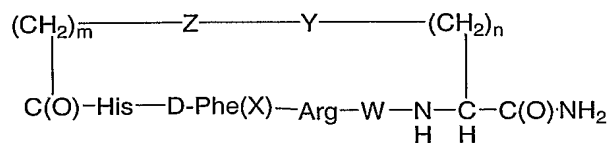
one of Y and Z is -C(O)- and the other is -NH-;

m is 1 to 4;

20 n is 1 to 4, provided that n+m is 4 to 6; or

a pharmaceutically acceptable salt thereof.

7. The method of Claim 6 wherein the compound of Formula I is selected from:



25

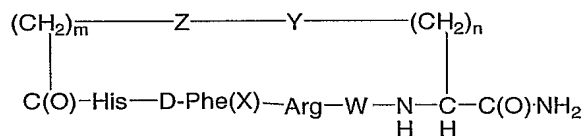
Z	Y	X	W	m	n
NH	C(O)	H	Trp	4	2
NH	C(O)	H	Trp	3	2
NH	C(O)	H	Trp	2	2
NH	C(O)	H	Trp	1	2

or a pharmaceutically acceptable salt thereof.

8. The method of Claim 7 wherein the compound of Formula I is selected from cyclo(NH-CH<sub>2</sub>-CH<sub>2</sub>-CO-His-D-Phe-Arg-Trp-Glu)-NH<sub>2</sub>, or a pharmaceutically acceptable salt thereof.

5

9. A method of treating alcoholism comprising administering a selective melanocortin 4 receptor agonist, or a pharmaceutically acceptable salt thereof, to a subject in need thereof wherein the selective melanocortin 4 receptor agonist is a compound of Formula I:



10

I

wherein:

His is L-histidyl;

D-Phe(X) is D-phenylalanyl unsubstituted or optionally para-substituted with a group selected from F, Cl, Br, Me, and OMe;

15 Arg is L-arginyl;

W is L-tryptophanyl or 2-naphthyl-L-alanyl;

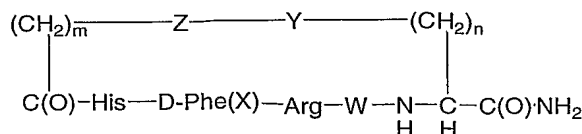
one of Y and Z is -C(O)- and the other is -NH-;

m is 1 to 4;

n is 1 to 4, provided that n+m is 4 to 6; or

20 a pharmaceutically acceptable salt thereof.

10. A method of treating alcohol abuse comprising administering a selective melanocortin 4 receptor agonist, or a pharmaceutically acceptable salt thereof, to a subject in need thereof wherein the selective melanocortin 4 receptor agonist is a compound of Formula I:



I

wherein:

His is L-histidyl;

5 D-Phe(X) is D-phenylalanyl unsubstituted or optionally para-substituted with a group selected from F, Cl, Br, Me, and OMe;

Arg is L-arginyl;

W is L-tryptophanyl or 2-naphthyl-L-alanyl;

one of Y and Z is -C(O)- and the other is -NH-;

10 m is 1 to 4;

n is 1 to 4, provided that n+m is 4 to 6; or

a pharmaceutically acceptable salt thereof.

11. A method of inhibiting alcohol consumption comprising administering to a subject in  
 15 need thereof a therapeutically effective amount of a selective melanocortin 4 receptor agonist, or a pharmaceutically acceptable salt thereof, with a functional activity characterized by an EC<sub>50</sub> at least 15-fold more selective for the human melanocortin 4 receptor than for the human melanocortin 1 receptor, the human melanocortin 3 receptor and the human melanocortin 5 receptor.

20 12. The method of Claim 11 wherein the functional activity of the melanocortin 4 receptor agonist is characterized by an EC<sub>50</sub> at least 17-fold more selective for the human melanocortin 4 receptor than for the human melanocortin 3 receptor.

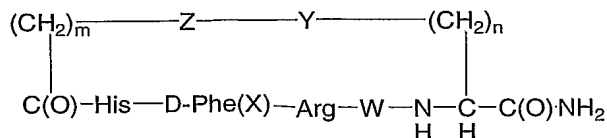
25 13. The method of Claim 11 wherein the functional activity of the melanocortin 4 receptor agonist is characterized by an EC<sub>50</sub> at least 90-fold more selective for the human melanocortin 4 receptor than for the human melanocortin 3 receptor.

30 14. The method of Claim 11 wherein the functional activity of the melanocortin 4 receptor agonist is characterized by an EC<sub>50</sub> at least 200-fold more selective for the human melanocortin 4 receptor than for the human melanocortin 5 receptor.

15. The method of Claim 11 wherein the functional activity of the melanocortin 4 receptor agonist is characterized by an EC<sub>50</sub> at least 3000-fold more selective for the human melanocortin 4

receptor than for the human melanocortin 5 receptor.

16. The use of a therapeutically effective amount of a melanocortin 4 receptor agonist of Formula I:



I

wherein:

His is L-histidyl;

D-Phe(X) is D-phenylalanyl unsubstituted or optionally para-substituted with a group selected from F,

Cl, Br, Me, and OMe;

Arg is L-arginyl;

W is L-tryptophanyl or 2-naphthyl-L-alanyl;

one of Y and Z is -C(O)- and the other is -NH-;

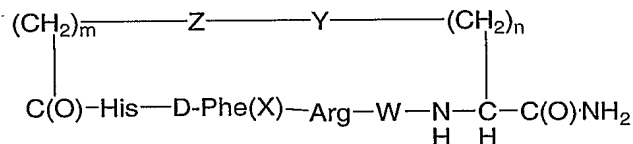
m is 1 to 4;

n is 1 to 4, provided that n+m is 4 to 6; or

a pharmaceutically acceptable salt thereof;

for the manufacture of a medicament useful to inhibit alcohol consumption in a subject in need of such treatment.

17. The use of a therapeutically effective amount of a melanocortin 4 receptor agonist of Formula I:



I

wherein:

His is L-histidyl;

D-Phe(X) is D-phenylalanyl optionally para-substituted with a group selected from F, Cl, Br, Me, and OMe;

Arg is L-arginyl;

W is L-tryptophanyl or 2-naphthyl-L-alanyl;

one of Y and Z is -C(O)- and the other is -NH-;

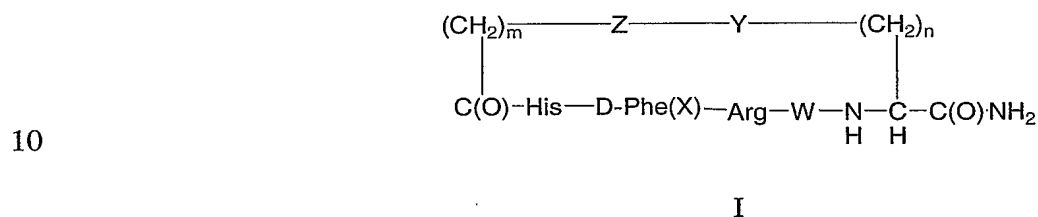
m is 1 to 4;

n is 1 to 4, provided that n+m is 4 to 6; or

a pharmaceutically acceptable salt thereof;

- 5 for the manufacture of a medicament useful to reduce alcohol consumption in a subject in need of such treatment.

18. The use of a therapeutically effective amount of a melanocortin 4 receptor agonist of Formula I:



wherein:

His is L-histidyl;

15 D-Phe(X) is D-phenylalanyl optionally para-substituted with a group selected from F, Cl, Br, Me, and OMe;

Arg is L-arginyl;

W is L-tryptophanyl or 2-naphthyl-L-alanyl;

one of Y and Z is -C(O)- and the other is -NH-;

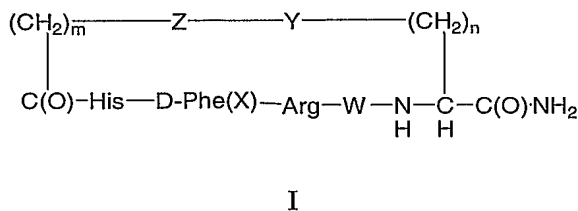
m is 1 to 4;

20 n is 1 to 4, provided that n+m is 4 to 6; or

a pharmaceutically acceptable salt thereof;

for the manufacture of a medicament useful to treat alcoholism in a subject in need of such treatment.

25 19. The use of a therapeutically effective amount of a melanocortin 4 receptor agonist of Formula I:



wherein:

His is L-histidyl;

D-Phe(X) is D-phenylalanyl optionally para-substituted with a group selected from F, Cl, Br, Me, and OMe;

Arg is L-arginyl;

W is L-tryptophanyl or 2-naphthyl-L-alanyl;

5 one of Y and Z is -C(O)- and the other is -NH-;

m is 1 to 4;

n is 1 to 4, provided that n+m is 4 to 6; or

a pharmaceutically acceptable salt thereof;

for the manufacture of a medicament useful to treat alcohol abuse in a subject in need of such treatment.

10